

# Epidemiological, anatomopathological and immunohistochemical profiles of male breast cancer in Sidi Bel Abbès, Algeria (Profiles of male breast cancer)

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## Abstract

### Background

Male breast cancer (BC) is a rare disease, few prospective studies have been undertaken compared to studies carried out in women. The condition is characterised by unfavorable prognosis when compared to that of females. The aim of the present work is to describe the anatomopathologic characteristics of males breast cancer at the level of the pathology department of the Hospital-University Center of Sidi Bel Abbès (ALGERIA).

### Methods

A descriptive cross-sectional study on male breast cancers diagnosed in our pathology department between January 2010 and December 2020 was undertaken, the variables assessed were epidemiological, macroscopic, microscopic and immunohistochemical data.

### Results

A total of 25 breast male cancer were identified in this study, the mean age at the diagnosis time was  $58.8 \pm 3.5$  years, and the age was ranging from 37 to 83. The mean tumor size was  $3.58 \pm 1.5$  cm, with sizeranging from 1.8 to 9 cm. About 18 of patients had tumors located in the upper outer quadrant (UOQ). Histopathological examination revealed the predominance of invasive carcinoma of no special type in 22 patients, followed by lobular carcinoma in 2 patients. 18 patients presented with nodal involvement and 23 of patients had hormonal receptors expression, including oestrogen receptor (RO), and progesterone receptor (RP). Additionnaly, just one patient had positive overexpression of HER2 (human epidermal growth factor receptor 2).

### Conclusion

Breast cancer in males in Algeria appears to be relatively rare and presents at an older age compared to females. Three out of four patients presented tumors in the UOQ and most were invasive carcinoma no special type. In the majority of male BC cases hormonal receptors and nodal involvement were present, while HER2 receptors were absent.

**KeyWords:** Males, breast, invasive carcinoma, hormonal receptors, overexpression of HER2, luminal A, luminal B.

## Introduction

Male BC is a rare pathology, it represents 0.6% of breast cancers<sup>1</sup>, and less than 1% of all male cancers<sup>2,3</sup>. This pathology is neglected making a late diagnosis which leads to relatively low survival rates<sup>4,5</sup>. Male breast cancer has many histopathological similarities to female BC<sup>6,7</sup>.

Etiopathogenesis is still unclear, however, imbalance between androgenic and estrogen hormones is the major factor that seems to be incriminated in breast cancer development<sup>8</sup>. The prognosis remains unfavourable compared to that of women. Due to the rarity of this pathology, few prospective studies of BC in males have been conducted. Thereby, the management recommendations are extrapolated from those applied for female breast cancers<sup>9,10,11</sup>. The immunohistochemical study shows a more significant hormone dependence of estrogen and progesterone receptors in men than in women<sup>12,13</sup>, as for the overexpression of Her2 in men remains low to that observed in women<sup>14,15</sup>.

The objective of this work is to describe the epidemiological, histopathological and immunohistochemical particularities of breast cancer in males diagnosed at the pathology department of the Hospital-University Center of Sidi Bel Abbès (ALGERIA).

## Methods

### *Type of study*

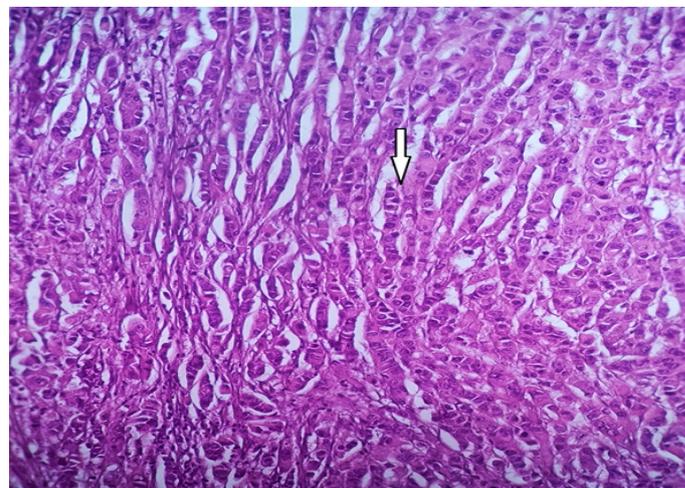
A retrospective descriptive study of male breast cancers was carried out in the pathology department of the Hospital-University Center of Sidi Bel Abbès, between January 1, 2010 to December 31, 2020.

### *Type of population and selection criteria*

All male with infiltrating breast cancer were eligible. Benign breast tumors ( lipoma, gynecomastia), carcinoma in situ of the ductal type and female cancers were excluded.

**Table 1: population characteristics**

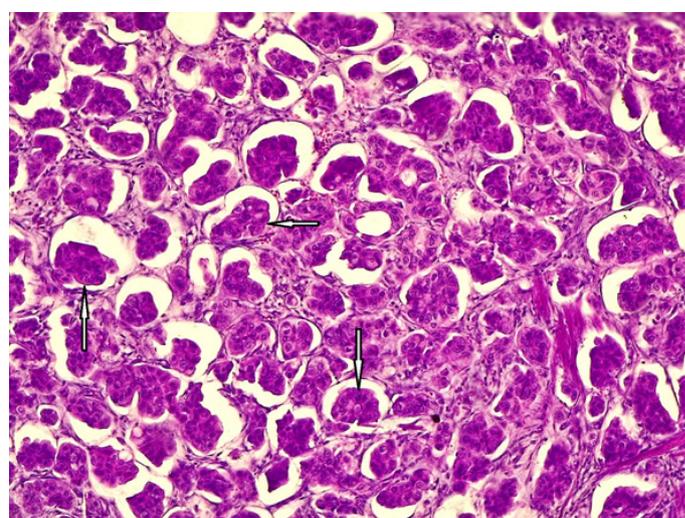
Variable	(n=25)
Side	
Left Breast	20
Right Breast	5
Age (years)	
Average	58.8 3.5
30-40	1
41-50	4
51-60	12
61-70	5
> 70	3



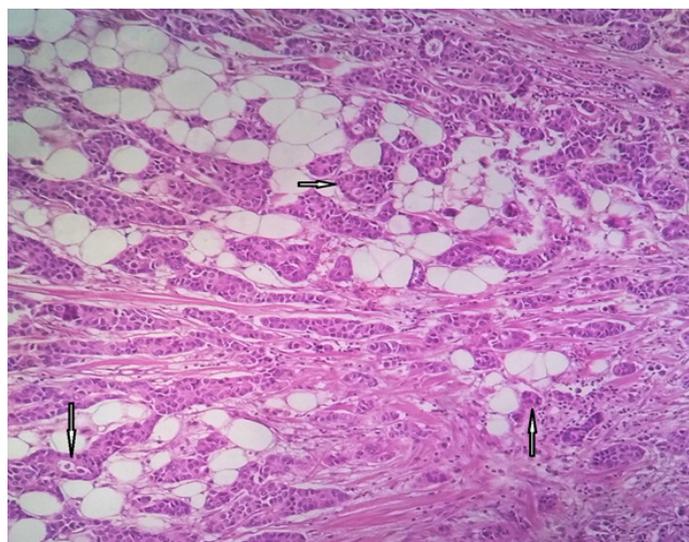
**Figure 3: microscopic showing of an invasive breast lobular carcinoma ( tumor cells arranged in single file, discohesive, small, monomorphic and lacking marked atypia), hematoxylin-eosin stains, X20.**



**Figure 1: left mastectomy piece fixed in 10% buffered formalin, oriented by 03 wires on the outer edge, 02 wires on the lower edge and 01 wire on the upper edge and centered by a nipple.**



**Figure 4: microscopic showing of an invasive breast micropapillary carcinoma ( tumor cells arranged in pseudopapillae and morula that are surrounded by empty clear spaces separated by thin fibrocollagenous stroma), hematoxylin-eosin stains, X10.**

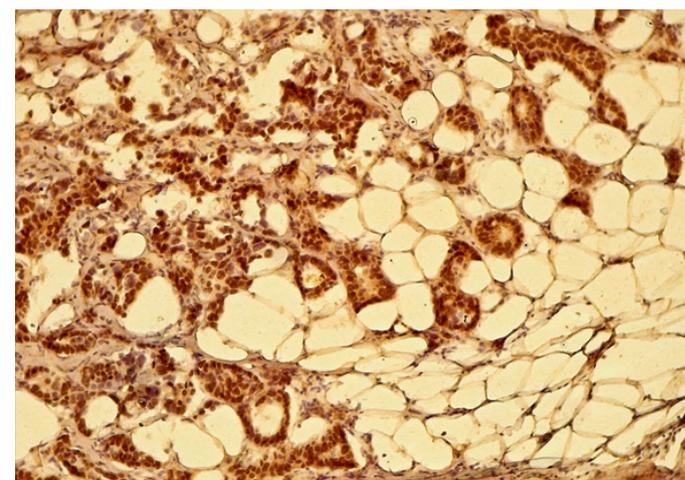


**Figure 2: microscopic showing of an invasive breast carcinoma of no special type infiltrating adipose tissue ( tumor cells arranged in glandular structures), hematoxylin-eosin stains, X10.**

**Data collection**

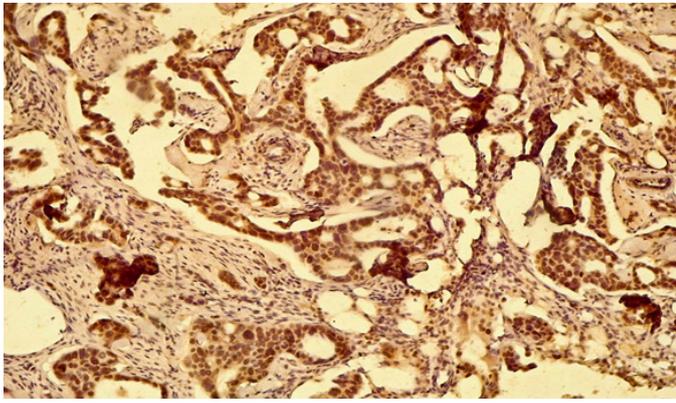
Data was collected from histopathological reports and included:

- Epidemiological data: age, side of the breast.
- Macroscopic data: nature of samples (biopsy or surgical specimen), location and tumor size.

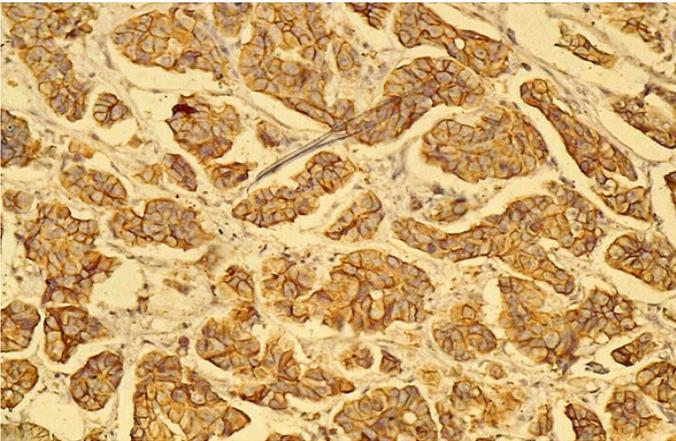


**Figure 5: microscopic showing strong nuclear labelling of tumor cells by the antibody (estrogen receptor), X20.**

- Microscopic data: histological type, Scarff-Bloom-Richardson (SBR) histoprognostic grade, resection margin and lymph node status.
- Immunohistochemical data: estrogen receptors (OR), progesterone receptors (PR), Her2 overexpression and Mib 1 proliferation index.



**Figure 6: microscopic showing strong nuclear labelling of tumor cells by the antibody (progesterone receptor), X20.**



**Figure 7: microscopic showing strong complete membrane labeling of tumor cells by the antibody (Herceptin 2), X20**

### Statistical analysis

All the data were processed and analyzed using SPSS software (Statistical Package For The Social Sciences) version 22. The statistical analysis was descriptive, calculating the absolute frequencies for the qualitative variables, for the quantitative variables, the mean and the extreme values.

### Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki preserving patient confidentiality and dignity. Patient names or other identifiers were not used in this study.

### Results

A total of 25 cases of male BC were analyzed in this current study, representing an annual frequency of 2.5 cases.

#### General characteristics of the study population

The average age was  $58.8 \pm 3.5$  years with extremes ranging from 37 to 83 years. About 12 cases were described in the age group between 51-60 years and only one case was under 40 years old. Left breast location was predominant with 20 cases versus 5 cases on the right breast (Table 1).

#### Macroscopic features

Diagnosis confirmation was made by surgical specimens (radical mastectomy with axillary dissection) in 20 cases [Figure 1], micro-biopsy appearances in 5 cases. The localisation in the UOQ was predominant in 18 cases, followed by the lower outer quadrant in 5 cases, the upper inner quadrant in 2 cases and no case was identified in the lower internal quadrant breast. The average tumor size was

$3.58 \pm 1.5$  cm with extremes ranging from 1.8 cm to 9 cm. About 16 patients had tumors classified pT2, 3 patients had tumors classified p T3 and one patient had a tumor classified p T1.

#### Histological type

The histological examination of the samples showed a clear predominance of invasive carcinoma no special type with 22 cases [Figure 2], followed by invasive lobular carcinoma with 2 cases [Figure 3] and invasive micropapillary carcinoma in one case [Figure 4]. According to the Scarf-Bloom-Richardson (SBR) classification, 21 of the patients were grade II, 4 patients were grade III and no grade I was reported. Furthermore, only one patient had positive surgical margins (R1), nodal invasion was found in 18 patients N(+), 2 patients N(-).

#### Immunohistochemical profile

The expression of the RO [Figure 5] and RP [Figure 6] hormone receptors were positive in 23 patients, 2 patients were negative. Her2 overexpression was positive in only one patient [Figure 7] and negative for the other patients. Concerning the subtypes, the luminal B profile was predominant in 20 patients, the luminal A profile was revealed in 3 patients, the Her2-amplified profile was found in one patient, and a single patient was triple negative.

#### Discussion

Male BC is a rare disease accounting for 0.5-1% of breast cancers in occidental countries<sup>16</sup> and 0.4-1.2% of male malignant neoplasias<sup>17</sup>. Its incidence has increased over the last 25 years<sup>18</sup>. The average age of diagnosis is 67 years, in the occidental countries<sup>17</sup> about 6 to 10 years later than in women<sup>19</sup>. In our sample, the age group most affected was 51-60 years with a mean average age of 58.8 years old. These results are in accordance with literature from elsewhere<sup>20,21,22,23</sup>. The left breast was the most affected (80%), which agrees with the study of Darre et al<sup>24</sup>.

In males, BC is frequently discovered at an advanced stage and the tumor size is often greater than that of tumors found in females<sup>25</sup>, this is explained by ignorance of the anatomy of the breast in male and the absence of organized screening targeting the male population. In our study, 95% of patients had tumors classified as T2, T3 with an average tumor size of 3.58 cm and a predominant location in the UOQ (72%), these results are consistent with data from the literature<sup>22,23,24,25,26,27,28</sup>.

According to data from the SEER (Surveillance, Epidemiology, and End Results cancer registry) invasive carcinoma of the no special type is the most frequent 93.7%, and lobular carcinoma represents 1.5%<sup>29</sup>. Our work reports similar results, in fact the percentage of invasive carcinoma of no special type in our study was 88%. Moreover, grade II SBR carcinoma were the majority of tumors with a rate of 84%. These results are comparable to international reports<sup>21,22,23,24,28</sup>. Lymph node status is a prognostic and predictive factor for metastatic relapse. In a multicenter analysis published by Cutili et al<sup>17</sup>, 53% of patients had lymph node involvement N+. However we found higher rates (90%), which could be explained by a delayed diagnosis. Radical surgical treatment such as mastectomy combined with axillary lymph node dissection or selective lymphadenectomy which remains the gold standard in early-stage cancers<sup>20,24,30,31</sup>. Lumpectomy procedure is not recommended because of the small size of

the mammary gland and the risk of passing into unhealthy areas<sup>31</sup>. In our present work, 20 patients underwent radical mastectomy with axillary lymph node dissection.

Hormone dependence shows a more significant expression of hormone receptors (RH) in males than in females<sup>32</sup>, according to the international standards, the positivity of HR ranged between 65% to 93%<sup>21,22,23,24,28</sup>, it accounted for 92% in our study. Overexpression of HER2 is less frequently found in males when compared to females and only 9% of male cancers are HER2+, in our analysis, only one patient had HER2+ status (4%), this result is similar to the literature findings<sup>30,33,34</sup>. Luminal type B was the predominant in our work, with a rate of 80% followed by luminal type A (12%), these observations are in accordance with several works where the majority of the cases corresponded either to the type luminal B or luminal A<sup>23,24,35</sup>.

This present study has limitations that must be taken into account when interpreting the results; firstly the small sample size does not confer enough statistical power and secondly it is a single center study whose results cannot be extrapolated to other sites. Nevertheless, it is considered as a pilot work for other studies in this pathology. Furthermore, the search for mutations of BRCA1, BRCA2 and the follow-up of patients were not carried out.

## Conclusion

In our study, breast cancer in males is determined at a later age than in females and at a more advanced stage. Three out of four patients presented tumors in the upper outer quadrant and most were invasive carcinoma no special type. Majority of male breast cancer presented with nodal involvement, hormonal receptors but not HER2 receptor. These results emphasize the necessity for a better optimization of breast cancer management.

## Conflict of interest

The authors declare no conflict of interest

## Author contribution

All the authors contributed equally in the manuscript. They approved the final and revised version of the manuscript.

## Acknowledgements

We would like to thank the Hospital-University Center of Sidi Bel Abbes for their permission to publish our study.

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